C L A I M S

1. Monoclonal antibody directed against the human interferon class I receptor (IFN-R) characterized by the following properties :
   - it recognizes the extracellular domain of the human IFN-R, and
   - it has a neutralizing capacity against the biological properties of the human type I-IFN.
2. Monoclonal antibody directed against the human type I IFN-R according to claim 1, characterized by its capacity to inhibit the binding of a human pathological type I-IFN, to the IFN-R.
3. Monoclonal antibody according to claim 1 or 2, which is obtainable from a hybridoma cell prepared by fusion of a myeloma cell with spleen cells from an animal previously immunized with the soluble form of the human IFN-R.
4. Monoclonal antibody according to anyone of claims 1, 2 or 3, characterized in that it recognizes an epitope on a soluble form of the human cellular IFN-R or of a recombinant IFN-R.
5. Monoclonal antibody according to anyone of claims 1 to 4, characterized in that it inhibits <u>in vitro</u> the binding of human type I-IFN, to the human cellular IFN-R when it is co-incubated with cells harboring the hu-IFN-R, at a concentration of antibodies equal or inferior to 100 µg/ml, preferably equal or inferior to 50 µg/ml, advantageously inferior to 20 µg/ml, more preferably in the range of approximately 0,5 to 2 µg/ml.
6. Monoclonal antibody according to anyone of claims 1 to 5, characterized in that it neutralizes <u>in vitro</u> the antiproliferative activity of the human type I-IFN, on cells highly responsive to this human type I-IFN,

for instance Daudi cells at a concentration in a range of 1 to 10 µg/ml.

7. Monoclonal antibody according to any ne of claims 1 to 6, characterized in that it neutralizes in vitro the antiproliferative activity of human type I-IFN, on cells poorly responsive to this human type I-IFN, for instance Ly28 cells, at a concentration in a range of 50 to 100 µg/ml.

8. Monoclonal antibody according to anyone of claims 1 to 7, characterized in that it does not bind to the human receptor of the IFN gamma.

9. Monoclonal antibody according to anyone of claims 1 to 8, characterized in that it recognizes an epitope on the aminoacid sequence 27 to 427 of the human IFN-R.

10. Monoclonal antibody according to anyone of claims 1 to 9, characterized in that it neutralizes in vitro the antiviral activity of the human type I-IFN, on cells highly responsive to this human type I-IFN, for instance Daudi cells at a concentration in a range of 1 to 10 µg/ml.

11. Monoclonal antibody according to anyone of claims 1 to 10, characterized in that it neutralizes in vitro the antiviral activity of the human class I-IFN, on cells poorly responsive to this human IFN, for instance Ly28 cells, at a concentration in a range of 50 to 100 µg/ml.

12. Monoclonal antibody according to anyone of claims 1 to 11, characterized in that it is the 64G12 antibody, deposited at the ECACC on February 26, 1992 under n° 92022605.

13. Monoclonal antibody according to anyone of claims 1 to 11, characterized in that it is a humanized antibody, for instance characterized in that the variable or complementary determining regions of its

heavy and light chains are grafted on the framework and constant regions of a human antibody.

14. Monoclonal antibody according to anyone of claims 1 to 11, characterized in that it is a human antibody.

15. Monoclonal antibody according to anyone of claims 1 to 11, characterized in that it is an IgG1 type antibody.

16. Hybridoma cell, characterized in that it produces monoclonal antibodies according to claims 1 to 13.

17. Composition having antagonist properties to the type I-IFN, characterized in that it comprises monoclonal antibodies according to anyone of claims 1 to 16.

18. Pharmaceutical composition, characterized in that it comprises monoclonal antibodies according to anyone of claims 1 to 17, together with an appropriate pharmaceutical vehicle.

19. Use of a monoclonal antibody according to anyone of claims 1 to 17, for the manufacture of a drug for the treatment or prophylaxis of a pathological state associated with proliferative cell activity and/or viral cell infection.

20. Process for the selection of a monoclonal antibody having the capacity to recognize the extracellular domain of the human IFN-R and capable of inhibiting the binding of the human type I-IFN, to the IFN-R, characterized by the following steps :

- preincubating a determined concentration of purified monoclonal antibodies according to anyone of claims 1 to 15 or a hybridoma culture supernatant containing monoclonal antibodies, with human cells susceptible of harboring IFN-R ;
- adding labelled human type I-IFN in a determined concentration, to the above preincubating medium ;

- incubating the medium c ntaining the human cells, monoclonal antibodies and labelled type I-IFN for a time sufficient to allow an equilibrium to occur, between the monoclonal antibodies on the one hand and the type I-IFN on the other hand, with the cellular IFN-R ;
- washing the cells ;
- determining the formation of a binding complex between the human cells and the type I-IFN, by counting the amount of attached labelled type I-IFN.

21. Process for the selection of a monoclonal antibody having the capacity to recognize the extra-cellular domain of the human IFN-R and having a neutralizing capacity against the antiproliferative activities of the type I-IFN, on human cells characterized by the steps of :

- allowing cells to grow in the presence of human type I-IFN and in the presence of a determined concentration of monoclonal antibodies according to anyone of claims 1 to 15 ;
- counting the cells in order to detect an inhibition of the antiproliferative effect of the type I-IFN.

22. Process for the selection of a monoclonal antibody having the capacity to recognize the extra-cellular domain of the human IFN-R and having a neutralizing capacity against the antiviral activities of the natural, non pathological or pathological type I-IFN on human cells, characterized by the steps of :

- incubating cells with type I-IFN and monoclonal antibodies according to anyone of claims 1 to 15, in determined concentrations, for a time sufficient to allow the formation of a complex

between the monoclonal antibodies and the IFN-R of th human cells and/ r between the type I-IFN and the IFN-R of the human cells ;

- infecting the above incubated cells with a determined concentration of a virus ;
- washing the cells ;
- resuspending the cells in culture medium ;
- incubating for a time sufficient to allow the replication of the virus ;
- lysing the cells and ;
- measuring the virus replication or measuring the inhibition of the cytopathic effect.

B1

add B1

add D2

add G8